



HISTOPATHOLOGICAL STUDY OF GASTRIC CANCER AT A TERTIARY MEDICAL CENTRE- A ONE YEAR EXPERIENCE.

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(ABSTRACT) Gastric cancer is very common worldwide and also in the North Eastern states of India. Histopathological examination is essential for its diagnosis, prognosis and treatment. The aim of this study was to assess the various histopathological features of gastric cancer specimens received at a tertiary medical centre of North East India. Among 31 patients who were studied, majority were males in their 5th decade. Antrum was the commonest site (70.96%); Adenocarcinoma was the commonest histology (93.5%); Tubular adenocarcinoma was the commonest subtype (82.76%); and most of the cases were Poorly differentiated (48.27%). Immunohistochemistry was utilized to diagnose a case of Non Hodgkin's Lymphoma. The results of this study compared well with those of previous studies. Because of its prominence, large scale epidemiological studies should be carried out in the North Eastern states to evaluate the various unique features of gastric cancer.

KEYWORDS : Gastric cancer, Histopathology, Adenocarcinoma

INTRODUCTION-

Gastric cancer remains the fourth most common type of cancer and is the second leading cause of cancer-related death worldwide^[1,2]. Although incidence has been steadily decreasing due to better prevention strategies, early diagnosis and better therapeutic interventions, but it still carries a poor prognosis because it's mostly diagnosed at a late stage^[3].

Histopathology has an important role in the management of stomach cancer because evaluation of endoscopically obtained tissue or a surgically resected specimen is essential for a diagnosis of cancer and also for prognostication.

The incidence of gastric cancer varies markedly with geography, both amongst separate countries and within different regions of a country itself^[4,6]. Different groups of population or communities in India show variations in the frequency of gastric cancer. The data obtained from the National Cancer Registries indicate that it is a leading problem in North-eastern and Southern states of the Indian subcontinent. The rates in North-eastern registries are higher than the rest of the country^[10]. There is paucity of analytical epidemiologic data on these cancers from India. Multi-center epidemiologic studies should be undertaken to solve some of the enigmas and observations peculiar to India^[11].

The following study was carried out in a teaching hospital of North-East India over a 1 year period to study the various histopathological characteristics of gastric cancers.

AIMS & OBJECTIVES- To study the various histopathological features of gastric cancers including their site and subtypes.

MATERIALS & METHODS-

It is a hospital based descriptive study and was carried out in the Department of Pathology of a Tertiary Medical Centre over a 1 year period from July 2013 to June 2014 with approval from the Institution Ethics Committee. A detailed informed consent was obtained from each patient. Surgically resected specimens & endoscopic biopsy specimens of stomach cancers were included in the study. Non neoplastic growths were excluded. Immunohistochemistry was done for evaluating only those cases which pose diagnostic difficulty with histopathology. All the patients in the present study were subjected to thorough history taking, full clinical examination and investigations.

Gross examination of the resected mass was done and its size, shape, consistency and other features noted. Sections were taken and tissue processing was done as per standard protocol. Staining was done with Hematoxylin and Eosin. For Immunohistochemistry, standard protocols were followed for processing and staining. Microscopic examination was then performed.

RESULTS & OBSERVATIONS-

A total of 31 cases were studied over a 1 year period (July 2013 to June 2014), of which 10 were surgically resected masses and 21 were endoscopic biopsies. In case of endoscopic biopsies the anatomical site was recorded from the endoscopic report.

The maximum number of gastric cancers (8 cases) was seen in the 6th decade. The mean age was 55.65 years. Males (18 cases) were more commonly affected than females (13 cases) with a ratio of 1.38: 1.

The following table shows the anatomical site of gastric cancers:

Table 1: showing anatomical location of gastric cancers

| Site | No. of cases | Percentage |
|--------|--------------|------------|
| Cardia | 1 | 3.23 |
| Fundus | 1 | 3.23 |
| Body | 7 | 22.58 |
| Antrum | 22 | 70.96 |
| Total | 31 | 100 |

The most common site was the Antrum (70.96%) followed by the Body (22.58%) of the stomach.

Majority of the gastric cancers were Adenocarcinomas (29 cases), and one case of GIST with high malignant potential and a single case of high grade Non Hodgkin's Lymphoma were seen.

Majority of the gastric cancers showed an Ulcerative growth pattern (17 cases) with an unusual case showing a large, exophytic, well circumscribed, lobulated mass arising from the body of the stomach, having dimensions of 14 cm x 11 cm x 12 cm; it was subsequently diagnosed as Gastrointestinal stromal tumour (GIST) of high malignant potential.

The following table shows the distribution of the various types of gastric adenocarcinomas:

Table 2- Types of gastric adenocarcinoma (WHO classification)

| Type | No. of cases | Percentage |
|---------------------------|--------------|------------|
| Tubular adenocarcinoma | 24 | 82.76 |
| Papillary adenocarcinoma | 2 | 6.90 |
| Poorly cohesive carcinoma | 2 | 6.90 |
| Mixed adenocarcinoma | 1 | 3.44 |
| Total | 29 | 100 |

The majority of gastric adenocarcinomas were Tubular adenocarcinomas (24 cases), according to WHO Classification. There were two cases each of Poorly cohesive carcinoma and Papillary adenocarcinoma. One case of Mixed adenocarcinoma was seen.

Most of the cancers were poorly differentiated (48.27%), followed by moderately differentiated (44.83%), and well differentiated types (6.9%).

One case of Gastrointestinal stromal tumour (GIST) was seen. Microscopically, it was composed of both epitheloid and spindle cell components, and it showed a mitotic rate of 2 per 50 high power fields. Thus a final diagnosis of GIST with high malignant potential was given.

One case was provisionally diagnosed as undifferentiated carcinoma and IHC was advised. On IHC, the neoplastic cells were CD45+ and CK- . Thus, a final diagnosis of High grade Non Hodgkin lymphoma (NHL) was given.

Fig.1- Well Differentiated Tubular Adenocarcinoma of Stomach (10X, H&E)

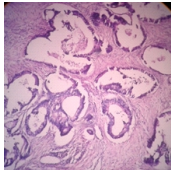


Fig.2- Poorly Differentiated Adenocarcinoma of Stomach (40X, H&E)

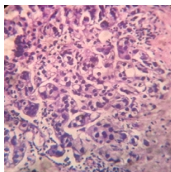


Fig.3- Papillary Adenocarcinoma Of Stomach (10X, H&E)-

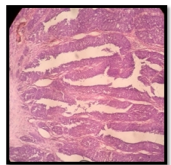


Fig.4- Poorly Cohesive Carcinoma of Stomach (40X, H&E)

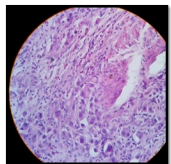


Fig.5- Diffuse Sheets of Neoplastic Cells In Gastric NHL (40X, H&E)

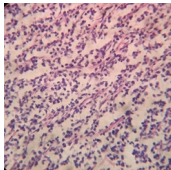


Fig.8- Positive Staining For CD45 in Gastric NHL (40X)

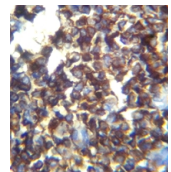
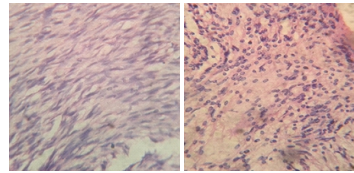


Fig.6- Gross Picture of Gastrointestinal Stromal Tumour (GIST) of Stomach



Fig.7- GIST Of Stomach, Mixed Type (Both Spindle & Epitheloid Components)-



DISCUSSION-

Gastric cancers have been known since ancient times. The Ebers Papyrus of 1500 BC possibly denotes the first mentions of gastric cancer. Hippocrates (460-375 BC) was the first to describe many cancers, including cancers of the stomach^[12].

It is an aggressive disease and has become a major global health burden^[3]. The median survival in patients with advanced and metastatic disease is less than 1 year^[13].

Early gastric cancer often causes no symptoms or only nonspecific symptoms like dyspepsia. Symptoms of advanced carcinoma include abdominal pain that is often persistent and unrelieved by eating. Ulcerated tumours may cause bleeding and haematemesis, and tumours that obstruct the gastric outlet may cause vomiting. Systemic symptoms such as anorexia and weight loss suggest disseminated disease. The lack of early symptoms often delays the diagnosis of gastric cancer^[7].

Salty, smoked or pickled foods have been associated with increased risk of developing gastric cancer^[8]. Gastro-esophageal reflux has been implicated in tumours of cardia and gastro-esophageal junction, whereas noncardia gastric cancers are strongly associated with chronic *H. pylori* infection^[5]. CDH1 (E-Cadherin) gene mutation is frequently responsible for here ditary and familial gastric cancers^[9].

Asia accounts for around 73% of gastric cancer cases; of which majority is in China^[3]. The data obtained from the National Cancer Registries indicate that gastric cancer is a leading problem in North-eastern and Southern states of the Indian subcontinent. North-eastern states of India have higher rates of gastric cancer than the rest of the country^[10].

The peak age group was 51-60 years, comprising 25.81% of all cases. The youngest patient was 24 years old, and the oldest patient was 92 years old. It compares with studies by Saha et al.,^[14] and Phukan et al.,^[6] in West Bengal and Mizoram respectively. In USA, the median age was found to be 71 years (Hayat et al.,)^[15] and it was 61 years in Japan^[16], which is slightly later than that seen in the present study. Males were commonly affected, and this correlates with studies by Phukan et al.,^[6] Harikumar et al.,^[17], Lee et al.,^[18], and Hansson et al.,^[19].

The antrum is the commonest site of gastric adenocarcinoma, but fundal involvement is increasing in recent years. Diffuse involvement of whole stomach is also not uncommon^[5]. The most common site of occurrence of gastric tumours in the present study was the antrum (70.96%), followed by the body of the stomach (25.8%) and this is similar to studies by Saha et al., (51.90%)^[14], and Zhou et al., (34%)^[20]. Many recent studies in other countries have also shown an increasing prevalence of involvement of the proximal stomach by gastric cancer^[21]. This difference may be due to racial, socio-cultural and environmental factors.

Grossly, the ulcerative growth pattern was commonly seen (58.62%) in the present study, which was similar to the study by Saha et al.,(57.80%)^[14].

Majority of the carcinomas in the present study were poorly differentiated type (48.27%), which is similar to that seen by Castellanos et al.,(57.50%)^[22] and Barad et al.,(44.30%)^[23].

Adenocarcinoma comprises over 90% of all gastric cancers. Primary gastric lymphoma, gastrointestinal stromal tumour (GIST) and carcinoids are rare^[4]. Adenocarcinoma was the commonest diagnosis (93.5%) in this study, and only one case of Non Hodgkin's Lymphoma (NHL) and a single case of GIST with high malignant potential was seen.

The WHO Classification divides gastric adenocarcinoma histologically into Tubular, Papillary, Mucinous and Poorly cohesive

(including signet ring cell carcinoma) types, and rare variants; among which Tubular adenocarcinoma is the commonest subtype, which is comparable to the present study^[24].

The Laurens Classification divides gastric cancers mainly into two types- Intestinal & Diffuse. The Intestinal type is more common than the diffuse type, whereas the diffuse variety is more aggressive and occurs at a relatively younger age^[3]. In our study the Intestinal variety was common and only two cases of diffuse gastric carcinoma were observed.

One case was diagnosed as undifferentiated carcinoma on microscopy, but on performing IHC the neoplastic cells were positive for CD45 and negative for cytokeratin (CK). Thus, the final diagnosis was gastric NHL.

Approximately, 90% of undifferentiated carcinomas can be accurately classified by exploiting immunohistochemistry, thus underlining the value of immunohistochemical procedures^[25].

H. pylori is strongly associated with the development of distal gastric cancer and its eradication has been shown to reduce the incidence of gastric cancer, but large scale eradication has not been supported by evidence, logistics, development of resistance and high rates of re-infection^[21]. Prophylactic gastrectomy is advised in patients with CDH1 germ-line mutations and family history of gastric cancer^[3].

Over-expression of Human epidermal growth factor receptor 2 (HER2), Epidermal growth factor receptor (EGFR) and Vascular endothelial growth factor A (VEGFA) is seen in gastric carcinoma. Molecular therapy targeting these specific genetic amplifications are already being used for treating advanced gastric cancer^[3].

CONCLUSION-

Gastric cancer remains one of the most frequently occurring and aggressive cancers worldwide. Histopathology of endoscopic biopsy and resected specimen still remains the standard for its diagnosis and confirmation. With current advances in molecular medicine, the role of histopathology including immunohistochemistry, for making therapeutic and prognostic decisions has only increased. As this disease has a very high incidence in North-East India, hence the current study which was undertaken in a tertiary care centre of the North-east will help to assess its histopathological characteristics in the study population.

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